REMARKS

Upon entry of this amendment, claims 1-3, 6-7, 22-28 and 31-33 are pending in the instant application. Claims 4-5 and 29-30 have been cancelled herein without prejudice or disclaimer. Claims 1 and 25 have been amended. Support for the claim amendments and new claims presented herein is found throughout the specification and in the claims as originally filed. For example, support for the amendments to claims 1 and 25 is found at least at page 36, paragraph **[0113]**, at least at page 37, paragraph **[0115]**, and in claim 4 as originally filed. Accordingly, no new matter has been added by the amendments presented herein.

Claim Rejections Under 35 U.S.C. § 112, First Paragraph

Enablement

Claims 1-7 and 22-33 have been rejected under 35 U.S.C. § 112, first paragraph for lack of enablement. In particular, the Examiner has indicated that "it would require undue experimentation of one skilled in the art to practice the claimed invention." (Office Action, page 5).

Applicants respectfully disagree with the Examiner. However, merely to expedite the prosecution, Applicants have amended the claims. In particular, claim 1 has been amended to recite a method of effectively treating nephritis, by selecting an animal in need of treatment for nephritis; and administering to the animal a therapeutically effective dose of a neutralizing antibody, or binding fragment thereof, that binds to platelet derived growth factor-DD (PDGF-DD), wherein the neutralizing antibody, or binding fragment thereof, neutralizes PDGF-DD-induced mitogenic activity, and wherein the neutralizing antibody, or binding fragment thereof, comprises fully human anti-PDGF-DD antibody mAb 6.4 or an antibody in the same antigen-binding bin as fully human anti-PDGF-DD antibody mAb 6.4 selected from fully human antibody mAb 1.9, 1.19, 1.22, and 1.29, and wherein the nephritis is selected from mesangial proliferative nephritis, mesangial proliferative glomerulonephritis and glomerular nephritis.

Claim 25, as amended, recites a method of effectively treating nephritis by selecting an animal in need of treatment for nephritis; and administering to the animal a therapeutically effective dose of a neutralizing antibody, or binding fragment thereof, that binds to platelet derived growth factor-DD (PDGF-DD), wherein the neutralizing antibody, or binding fragment

thereof, neutralizes PDGF-DD-induced mitogenic activity, and wherein the neutralizing antibody, or binding fragment thereof comprises fully human anti-PDGF-DD antibody mAb 6.4 or an antibody in the same antigen-binding bin as fully human anti-PDGF-DD antibody mAb 6.4 selected from fully human antibody mAb 1.9, 1.19, 1.22, and 1.29 and wherein the neutralizing antibody, or binding fragment thereof, comprises a fully human IgG2 heavy chain, and wherein the nephritis is selected from mesangial proliferative nephritis, mesangial proliferative glomerulonephritis and glomerular nephritis.

Applicants submit that the amended claims presented herein are enabled by the instant specification. As acknowledged by the Examiner on page 2 of the Office Action, the specification is enabling for "a method of treating mesangial cell proliferative nephritis or glomerulonephritis comprising selecting an animal in need of treatment for nephritis; and administering to the animal a therapeutically effective dose of a neutralizing antibody mAb 6.4 or binding fragment thereof that binds specifically to either mouse or human platelet derived growth factor-DD (PDGF-DD), wherein the neutralizing antibody or binding fragment thereof neutralizes PDGF-DD-induced mitogenic activity of mesangial cell".

In addition, Applicants submit that the specification is enabling for a method of treating mesangial cell proliferative nephritis, mesangial proliferative glomerulonephritis or glomerulonephritis using an antibody in the same antigen-binding bin as fully human anti-PDGF-DD antibody mAb 6.4 selected from fully human antibody mAb 1.9, 1.19, 1.22, and 1.29. As described above, amended claims 1 and 25 are not directed to any antibody in the same antigen-binding bin as mAb 6.4. Rather, these claims recite a specific subset of antibodies in the same antigen-binding bin as mAb 6.4. These "binned" antibodies are disclosed, *e.g.*, in PCT Publication WO 03/057857, published on July 17, 2003, expressly incorporated by reference in the instant application at page 36, paragraph **[0113]**.

Thus, Applicants submit that a person of ordinary skill in the art, with the specification in hand and given the state of the art at the time of filing, could make and use the claimed methods of treating nephritis without undue experimentation.

In view of the foregoing, Applicants respectfully request that the rejections under 35 U.S.C. § 112, first paragraph, for lacking of enablement, be withdrawn.

Written Description

Claims 1-7 and 22-33 have also been rejected under 35 U.S.C. § 112, first paragraph for lack of written description. According to the Examiner, the specification "does not provide a written description of any anti-PDGF-DD or binding fragment thereof that 'cross-reacts' with fully human anti-PDGF-DD antibody or mAb 6.4 or any anti-PDGF-DD or binding fragment thereof in the same 'antigen-binding bin' as fully human anti-PDGF-DD antibody mAb 6.4 that is effective in treating any nephritis." (Office Action, page 5).

As described above, the pending claims have been amended herein. The claimed methods are described throughout the specification and in the claims as originally filed. For example, the antibodies recited by amended claims 1 and 25 are disclosed in the specification at least at page 36, paragraph **[0113]** and at least at page 37, paragraph **[0115]**, while the nephritis disorders recited by the amended claims are disclosed, *e.g.*, at page 5, paragraph **[0013]**, at pages 5-6, paragraph **[0015]**, throughout the Examples, and in claim 4 as originally filed.

Thus, the disclosure provided throughout the as-filed specification is commensurate with the scope of the amended claims presented herein. Accordingly, Applicant submits that the specification provides sufficient written description of the claimed polypeptides so as to reasonably convey to one skilled in the relevant art that the inventors had possession of the claimed invention at the time the instant application was filed. As such, this rejection should be withdrawn.

Claim Rejections Under 35 U.S.C. § 112, Second Paragraph

Claim 1 has been rejected under 35 U.S.C. § 112, second paragraph, as being indefinite. In particular, the Examiner has stated that the term "antigen-binding bin" in claim 1 is "ambiguous and indefinite because one of ordinary skill in the art cannot apprise the metes and bounds of the claimed invention." (Office Action, page 7).

Applicants submit that the term "antigen-binding bin" is defined in the specification at page 37, paragraph **[0115]** and in the published PCT application expressly incorporated by reference in this paragraph, WO 03/048731, entitled "Antibody Categorization Based on Binding Characteristics". (*See e.g.*, WO 03/048731 at page 20, lines 20-24). Moreover, claim 1 has been amended to recite antibody in the same antigen-binding bin as fully human anti-PDGF-DD

antibody mAb 6.4 selected from fully human antibody mAb 1.9, 1.19, 1.22, and 1.29. Accordingly, Applicants submit that the metes and bounds of this amended claim are clear and definite. As such, withdrawal of this rejection is requested.

Claim Rejections Under 35 U.S.C. § 102(b)

The Examiner has rejected claims 1-2, 4-5 and 22 under 35 U.S.C. § 102(b) as being anticipated by Johnson *et al.*, J. Exp. Med., vol. 175:1413-1416 (1992) ("Johnson"). According to the Examiner, Johnson describes "a method of treating nephritis such as mesangial cells proliferative glomerulonephritis by administering via injection to the animal such as Wistar rats induced anti-Thy-1 ... a neutralizing polyclonal antibody that binds to and neutralized all dimeric forms of PDGF." (Office Action, page 7).

As described above, claim 1 has been amended to recite a method of effectively treating nephritis, by selecting an animal in need of treatment for nephritis; and administering to the animal a therapeutically effective dose of a neutralizing antibody, or binding fragment thereof, that binds to platelet derived growth factor-DD (PDGF-DD), wherein the neutralizing antibody, or binding fragment thereof, neutralizes PDGF-DD-induced mitogenic activity, and wherein the neutralizing antibody, or binding fragment thereof, comprises fully human anti-PDGF-DD antibody mAb 6.4 or an antibody in the same antigen-binding bin as fully human anti-PDGF-DD antibody mAb 6.4 selected from fully human antibody mAb 1.9, 1.19, 1.22, and 1.29, and wherein the nephritis is selected from mesangial proliferative nephritis, mesangial proliferative glomerulonephritis and glomerular nephritis.

In contrast to the claimed methods, Johnson does not teach or suggest the use of the fully human anti-PDGF-DD antibody mAb 6.4 or an antibody in the same antigen-binding bin as fully human anti-PDGF-DD antibody mAb 6.4 selected from fully human antibody mAb 1.9, 1.19, 1.22, and 1.29. Accordingly, Johnson fails to disclose or suggest every element of the claimed invention. As such, claim 1 and its dependent claims (including claims 2 and 22) are novel over this reference, and this rejection should be withdrawn.

Claim Rejections Under 35 U.S.C. § 103(a)

Claims 1, 3 and 23-30

The Examiner has rejected claims 1, 3 and 23-30 under 35 U.S.C. § 103(a) as being unpatentable over Johnson in view of LaRochelle *et al.*, Nature Cell Biol., vol. 3:517-21 ("LaRochelle") and PCT Publication No. WO 96/34096 by Kucherlapati *et al.* ("Kucherlapati"), or U.S. Pat. No. 6,207,418 by Hori *et al.* ("Hori"). According to the Examiner, "it would have been obvious to one of ordinary skill in the art at the time the invention was made to make any fully human antibody that binds to any antigen of interest as taught by the WO 96/34096 publication or the '418 patent having a human IgG2 heavy chain using the human or mouse PDGF-DD as taught by LaRochelle et al for a method of treating nephritis as taught by Johnson et al." (Office Action, page 9).

Claim 1 has been amended to recite a method of effectively treating nephritis, by selecting an animal in need of treatment for nephritis; and administering to the animal a therapeutically effective dose of a neutralizing antibody, or binding fragment thereof, that binds to platelet derived growth factor-DD (PDGF-DD), wherein the neutralizing antibody, or binding fragment thereof, neutralizes PDGF-DD-induced mitogenic activity, and wherein the neutralizing antibody, or binding fragment thereof, comprises fully human anti-PDGF-DD antibody mAb 6.4 or an antibody in the same antigen-binding bin as fully human anti-PDGF-DD antibody mAb 6.4 selected from fully human antibody mAb 1.9, 1.19, 1.22, and 1.29, and wherein the nephritis is selected from mesangial proliferative nephritis, mesangial proliferative glomerulonephritis and glomerular nephritis.

As described above, Johnson fails to teach or suggest the use of the fully human anti-PDGF-DD antibody mAb 6.4 or an antibody in the same antigen-binding bin as fully human anti-PDGF-DD antibody mAb 6.4 selected from fully human antibody mAb 1.9, 1.19, 1.22, and 1.29. The addition of the LaRochelle, Kucherlapati and Hori references fail to remedy the deficiencies of the Johnson reference, as these references, alone or in combination, do not disclose or suggest methods of treating nephritis using these particular antibodies. Accordingly, the pending claims, as amended, are not obvious in view of these references. Withdrawal of this rejection is, therefore, requested.

Claims 1 and 6-7

Claims 1 and 6-7 have also been rejected under 35 U.S.C. § 103(a) as being unpatentable over Johnson in view of U.S. Patent No. 6,706,687 by Eriksson *et al.* ("Eriksson"). The Examiner has indicated that "it would have been obvious to one of ordinary skill in the art at the time the invention was made to administer anti-PDGF-DD antibody for treatment of nephritis as taught by Johnson et al via subcutaneous or muscular injection as taught by the '687 patent". (Office Action, page 10).

Claims 6-7 depend from claim 1, which has been amended as described above. In contrast to the claimed methods, Johnson does not disclose or suggest the use of the fully human anti-PDGF-DD antibody mAb 6.4 or an antibody in the same antigen-binding bin as fully human anti-PDGF-DD antibody mAb 6.4 selected from fully human antibody mAb 1.9, 1.19, 1.22, and 1.29. The addition of the Eriksson reference fails remedy the deficiencies of the Johnson reference, as this reference does not teach or suggest methods of treating nephritis using any of the fully human antibodies selected from mAb 6.4, 1.9, 1.19, 1.22, or 1.29. Accordingly, amended claim 1 and its dependent claims (including claims 6-7) are not obvious over the Johnson and Eriksson references, either alone or in combination. As such, this rejection should be withdrawn.

Claims 31 and 32

Claims 31 and 32 have also been rejected under 35 U.S.C. § 103(a) as being unpatentable over Johnson in view of LaRochelle and Kucherlapati or Hori and in further view of Eriksson. The Examiner has indicated that "it would have been obvious to one of ordinary skill in the art at the time the invention was made to administer fully human anti-PDGF-DD antibody comprising human IgG2 heavy chain and human kappa light chain as taught by [LaRochelle, Kucherlapati or Hori] for the treatment of nephritis as taught by Johnson et al via subcutaneous or muscular injection as taught by the '687 patent". (Office Action, page 11).

Claims 31 and 32 depend from claim 25, which has been amended to recite a method of effectively treating nephritis by selecting an animal in need of treatment for nephritis; and administering to the animal a therapeutically effective dose of a neutralizing antibody, or binding fragment thereof, that binds to platelet derived growth factor-DD (PDGF-DD), wherein the neutralizing antibody, or binding fragment thereof, neutralizes PDGF-DD-induced mitogenic

activity, and wherein the neutralizing antibody, or binding fragment thereof comprises fully human anti-PDGF-DD antibody mAb 6.4 or an antibody in the same antigen-binding bin as fully human anti-PDGF-DD antibody mAb 6.4 selected from fully human antibody mAb 1.9, 1.19, 1.22, and 1.29 and wherein the neutralizing antibody, or binding fragment thereof, comprises a fully human IgG2 heavy chain, and wherein the nephritis is selected from mesangial proliferative nephritis, mesangial proliferative glomerulonephritis and glomerular nephritis.

The Johnson reference, however, fails to describe or suggest the use of the fully human anti-PDGF-DD antibody mAb 6.4 or an antibody in the same antigen-binding bin as fully human anti-PDGF-DD antibody mAb 6.4 selected from fully human antibody mAb 1.9, 1.19, 1.22, and 1.29 for the treatment of nephritis. The Kucherlapati, Hori and Eriksson references fail to remedy the deficiencies in the teachings of the Johnson reference, as these references, alone or in combination, fail to disclose or suggest methods of treating nephritis using these particular antibodies. As such, Applicants respectfully request that this rejection be withdrawn.

Claims 33

Claim 33 has been rejected under 35 U.S.C. § 103(a) as being unpatentable over Johnson in view of LaRochelle and Kucherlapati or Hori and in further view of U.S. Patent No. 6,630,142 by Hart *et al.* ("Hart"). According to the Examiner, "it would have been obvious to one of ordinary skill in the art at the time the invention was made to determine the antibody binding affinity (Kd) by Scatchard analysis as taught by the '142 patent using the fully human antibody that binds specifically to PDGF-DD comprising human IgG2 heavy chain and human kappa light chain as taught by [LaRochelle, Kucherlapati, and Hori] with the expectation that the binding affinity or kD in the range of at least 10^{-6} M for a method of treating nephritis as taught by Johnson et al." (Office Action, page 12).

Claim 33 depends from claim 25, which has been amended, as described above. Johnson, however, does not disclose or suggest the use of the fully human anti-PDGF-DD antibody mAb 6.4 or an antibody in the same antigen-binding bin as fully human anti-PDGF-DD antibody mAb 6.4 selected from fully human antibody mAb 1.9, 1.19, 1.22, and 1.29 for the treatment of nephritis, as recited by amended claim 25. The addition of the LaRochelle, Kucherlapati, Hori and Hart references fail to remedy the deficiencies of the Johnson reference, as these references do not teach or suggest methods of treating nephritis using any of the fully human antibodies

selected from mAb 6.4, 1.9, 1.19, 1.22, or 1.29. Accordingly, amended claim 25 and its dependent claims (including claim 33) are not obvious over the cited references, either alone or in combination. As such, this rejection should be withdrawn.

CONCLUSION

Applicants respectfully submit that the pending claims are in condition for allowance. If there are any questions regarding these amendments and remarks, the Examiner is encouraged to contact the undersigned at the telephone number provided below.

Respectfully submitted,

38,384

Ivor R. Elrifi, Reg. No. 39,529
Attorney for Applicant
c/o MINTZ, LEVIN
Tel: (617) 542-6000
Fax: (617) 542-2241
Customer No. 55111

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